Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

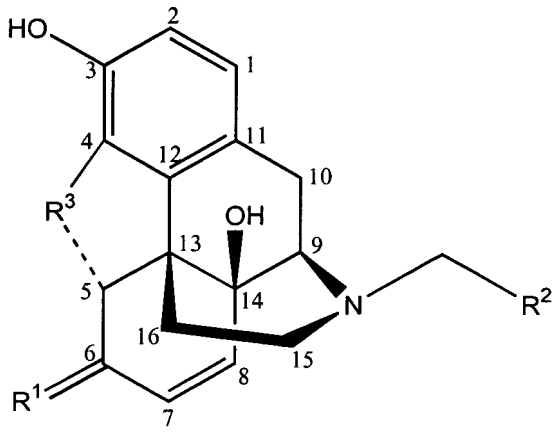
Claim 1 (withdrawn). A method of enhancing efficacy of a non-opioid CNS-active agent comprising:

co-administering to a patient a therapeutic dose of the non-opioid CNS-active agent and an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter.

Claim 2 (withdrawn). The method of claim 1, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 3 (withdrawn). The method of claim 2, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 4 (withdrawn). The method of claim 1, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 5 (withdrawn). The method of claim 1, wherein the drug transporter is a P-glycoprotein.

Claim 6 (withdrawn). The method of claim 5, wherein the P-glycoprotein is PGP1a.

Claim 7 (withdrawn). The method of claim 1, further comprising administering to the patient an opioid receptor agonist.

Claim 8 (withdrawn). The method of claim 7, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 9 (withdrawn). The method of claim 8, wherein the adverse side effect is constipation.

Claim 10 (withdrawn). The method of claim 1, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 11 (withdrawn). The method of claim 1, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

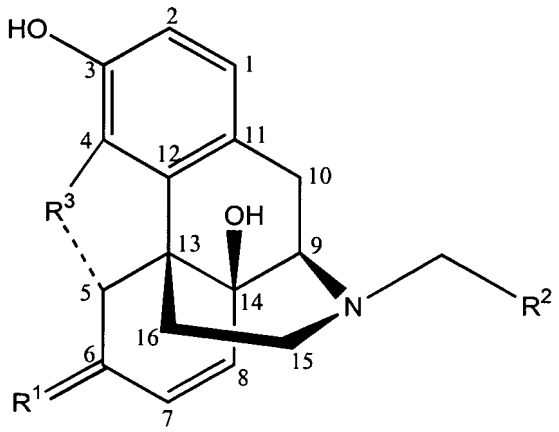
Claim 12 (withdrawn). A method of enhancing efficacy of a non-opioid CNS-active agent comprising:

co-administering to a patient a sub-therapeutic dose of the non-opioid CNS-active agent and an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter.

Claim 13 (withdrawn). The method of claim 12, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 14 (withdrawn). The method of claim 13, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 15 (withdrawn). The method of claim 12, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 16 (withdrawn). The method of claim 12, wherein the drug transporter is a P-glycoprotein.

Claim 17 (withdrawn). The method of claim 16, wherein the P-glycoprotein is PGP1a.

Claim 18 (withdrawn). The method of claim 12, further comprising administering to the patient an opioid receptor agonist.

Claim 19 (withdrawn). The method of claim 18, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 20 (withdrawn). The method of claim 19, wherein the adverse side effect is constipation.

Claim 21 (withdrawn). The method of claim 12, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 22 (withdrawn). The method of claim 12, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

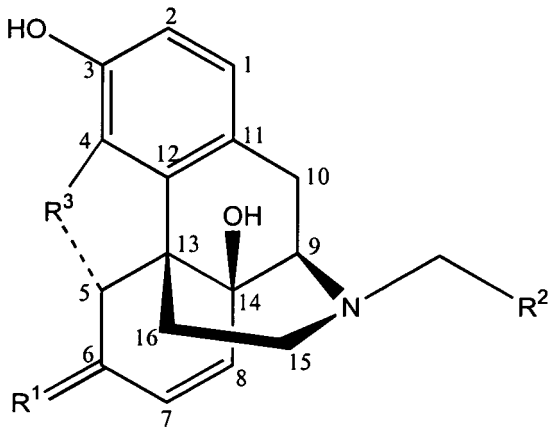
Claim 23 (withdrawn). A method of enhancing efficacy of a non-opioid CNS-active agent comprising:

co-administering to a patient a therapeutic dose of the non-opioid CNS-active agent and an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter.

Claim 24 (withdrawn). The method of claim 23, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 25 (withdrawn). The method of claim 24, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 26 (withdrawn). The method of claim 23, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 27 (withdrawn). The method of claim 23, wherein the drug transporter is a P-glycoprotein.

Claim 28 (withdrawn). The method of claim 27, wherein the P-glycoprotein is PGP1a.

Claim 29 (withdrawn). The method of claim 23, further comprising administering to the patient an opioid receptor agonist.

Claim 30 (withdrawn). The method of claim 29, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 31 (withdrawn). The method of claim 30, wherein the adverse side effect is constipation.

Claim 32 (withdrawn). The method of claim 23, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 33 (withdrawn). The method of claim 23, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

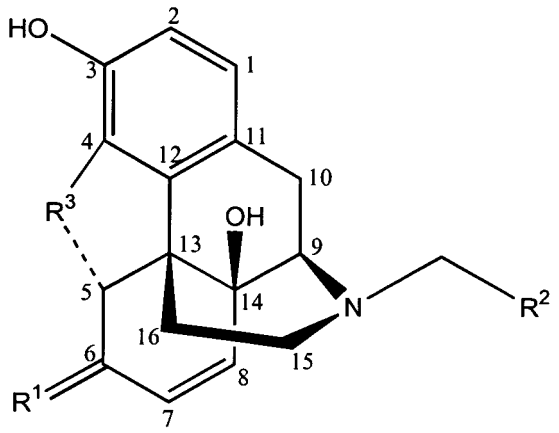
Claim 34 (withdrawn). A method of enhancing efficacy of a non-opioid CNS-active agent comprising:

co-administering to a patient a sub-therapeutic dose of the non-opioid CNS-active agent and an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter.

Claim 35 (withdrawn). The method of claim 34, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 36 (withdrawn). The method of claim 35, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 37 (withdrawn). The method of claim 34, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 38 (withdrawn). The method of claim 34, wherein the drug transporter is a P-glycoprotein.

Claim 39 (withdrawn). The method of claim 38, wherein the P-glycoprotein is PGP1a.

Claim 40 (withdrawn). The method of claim 34, further comprising administering to the patient an opioid receptor agonist.

Claim 41 (withdrawn). The method of claim 40, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 42 (withdrawn). The method of claim 41, wherein the adverse side effect is constipation.

Claim 43 (withdrawn). The method of claim 34, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 44 (withdrawn). The method of claim 34, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 45 (withdrawn). A method of reversing tolerance to a non-opioid CNS-active agent comprising co-administering to a patient who is tolerant to the non-opioid CNS-active agent :

(a) an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter, and

(b) the non-opioid CNS-active agent to which the patient developed tolerance.

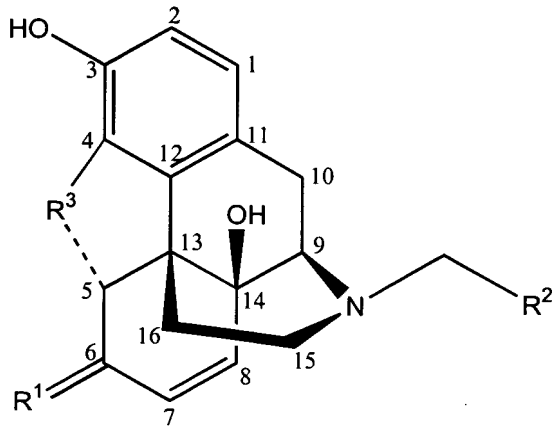
Claim 46 (withdrawn). The method of claim 45, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 47 (withdrawn). The method of claim 46, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 48 (withdrawn). The method of claim 45, wherein the drug transporter is a P-glycoprotein.

Claim 49 (withdrawn). The method of claim 48, wherein the P-glycoprotein is PGP1a.

Claim 50 (withdrawn). The method of claim 45, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

Claim 51 (withdrawn). The method of claim 45, further comprising administering to the patient an opioid receptor agonist.

Claim 52 (withdrawn). The method of claim 51, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 53 (withdrawn). The method of claim 52, wherein the adverse side effect is constipation.

Claim 54 (withdrawn). The method of claim 45, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 55 (withdrawn). The method of claim 45, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 56 (withdrawn). A method of reversing tolerance to a non-opioid CNS-active agent comprising co-administering to a patient who is tolerant to the non-opioid CNS-active agent:

(a) an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter, and

(b) the non-opioid CNS-active agent to which the patient developed tolerance.

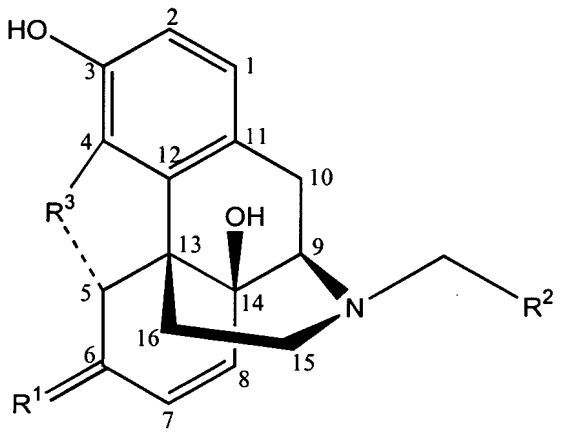
Claim 57 (withdrawn). The method of claim 56, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 58 (withdrawn). The method of claim 57, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 59 (withdrawn). The method of claim 56, wherein the drug transporter is a P-glycoprotein.

Claim 60 (withdrawn). The method of claim 59, wherein the P-glycoprotein is PGP1a.

Claim 61 (withdrawn). The method of claim 56, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 62 (withdrawn). The method of claim 56, further comprising administering to the patient an opioid receptor agonist.

Claim 63 (withdrawn). The method of claim 62, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 64 (withdrawn). The method of claim 63, wherein the adverse side effect is constipation.

Claim 65 (withdrawn). The method of claim 56, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 66 (withdrawn). The method of claim 56, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 67 (withdrawn). A method of treating a patient with chronic pain comprising:

repeatedly over a period of time, co-administering to a patient a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent and an amount of an inhibitor of drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain;

wherein the period of time is greater than the period of time in which the patient would develop tolerance to or develop dependence upon the non-opioid CNS-active

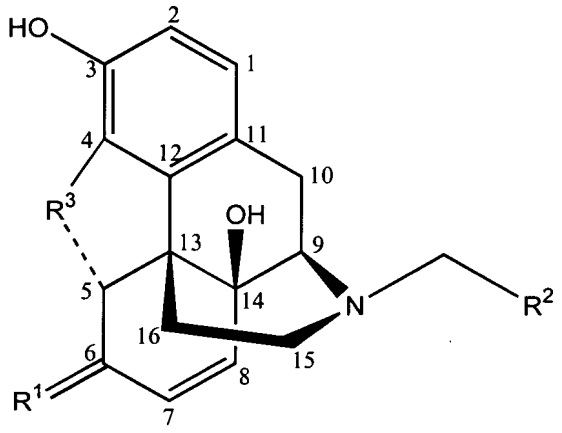
agent administered in the absence of the inhibitor of the drug transporter, and wherein the drug transporter is an ABC drug transporter.

Claim 68 (withdrawn). The method of claim 67, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 69 (withdrawn). The method of claim 68, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 70 (withdrawn). The method of claim 67, further comprising administering to the patient an opioid receptor agonist.

Claim 71 (withdrawn). The method of claim 67, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 72 (withdrawn). The method of claim 67, wherein the period of time is greater than the period of time in which the patient would develop tolerance to the non-opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 73 (withdrawn). The method of claim 67, wherein the period of time is greater than the period of time in which the patient would develop dependence upon the non-opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 74 (withdrawn). The method of claim 67, wherein the drug transporter is a P-glycoprotein.

Claim 75 (withdrawn). The method of claim 74, wherein the P-glycoprotein is PGP1a.

Claim 76 (withdrawn). The method of claim 75, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 77 (withdrawn). The method of claim 76, wherein the adverse side effect is constipation.

Claim 78 (withdrawn). The method of claim 67, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 79 (withdrawn). The method of claim 67, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 80 (withdrawn). A method of treating a patient with chronic pain comprising:

repeatedly over a period of time, co-administering to a patient a therapeutic or sub-therapeutic dose of an non-opioid CNS-active agent and an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain;

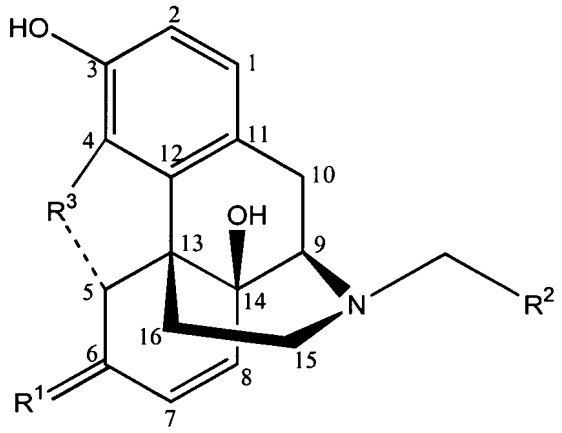
wherein the period of time is greater than the period of time in which the patient would develop tolerance to or develop dependence upon the non-opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter, and wherein the drug transporter is an ABC drug transporter.

Claim 81 (withdrawn). The method of claim 80, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 82 (withdrawn). The method of claim 81, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 83 (withdrawn). The method of claim 80, further comprising administering to the patient an opioid receptor agonist.

Claim 84 (withdrawn). The method of claim 80, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 85 (withdrawn). The method of claim 80, wherein the period of time is greater than the period of time in which the patient would develop tolerance to upon the non-opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 86 (withdrawn). The method of claim 80, wherein the period of time is greater than the period of time in which the patient would develop dependence upon the non-opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 87 (withdrawn). The method of claim 80, wherein the drug transporter is a P-glycoprotein.

Claim 88 (withdrawn). The method of claim 87, wherein the P-glycoprotein is PGP1a.

Claim 89 (withdrawn). The method of claim 88, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 90 (withdrawn). The method of claim 89, wherein the adverse side effect is constipation.

Claim 91 (withdrawn). The method of claim 80, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 92 (withdrawn). The method of claim 80, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 93 (withdrawn). A method of controlling chronic pain without dependence upon a CNS-active agent comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing dependence upon the CNS-active agent, and wherein the drug transporter is an ABC drug transporter.

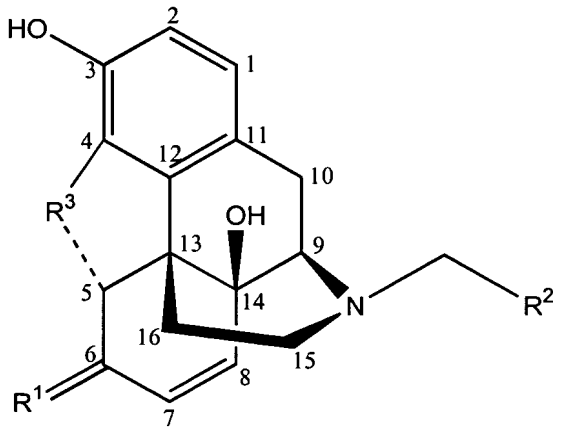
Claim 94 (withdrawn). The method of claim 93, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 95 (withdrawn). The method of claim 94, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 96 (withdrawn). The method of claim 93, further comprising administering to the patient an opioid receptor agonist.

Claim 97 (withdrawn). The method of claim 93, wherein the therapeutic or sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop dependence upon the non-opioid CNS-active agent.

Claim 98 (withdrawn). The method of claim 93, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 99 (withdrawn). The method of claim 93, wherein the drug transporter is a P-glycoprotein.

Claim 100 (withdrawn). The method of claim 99, wherein the P-glycoprotein is PGP1a.

Claim 101 (withdrawn). The method of claim 96, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 102 (withdrawn). The method of claim 101, wherein the adverse side effect is constipation.

Claim 103 (withdrawn). The method of claim 93, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 104 (withdrawn). The method of claim 93, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 105 (withdrawn). A method of controlling chronic pain without dependence upon a CNS-active agent comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing dependence upon the CNS-active agent, and wherein the drug transporter is an ABC drug transporter.

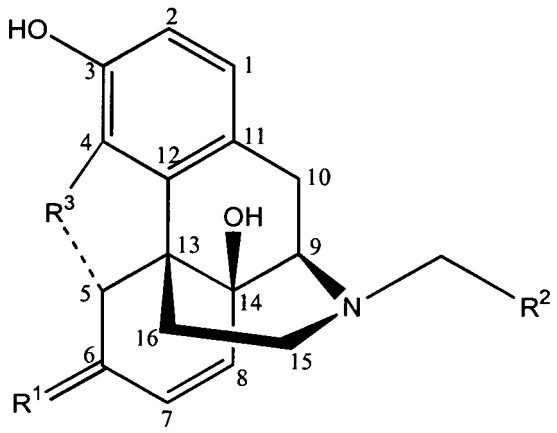
Claim 106 (withdrawn). The method of claim 105, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 107 (withdrawn). The method of claim 106, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 108 (withdrawn). The method of claim 105, further comprising administering to the patient an opioid receptor agonist.

Claim 109 (withdrawn). The method of claim 105, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop a drug dependence upon the non-opioid CNS-active agent.

Claim 110 (withdrawn). The method of claim 105, wherein the inhibitor of the drug transporter is is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

Claim 111 (withdrawn). The method of claim 105, wherein the drug transporter is a P-glycoprotein.

Claim 112 (withdrawn). The method of claim 111, wherein the P-glycoprotein is PGP1a.

Claim 113 (withdrawn). The method of claim 108, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 114 (withdrawn). The method of claim 113, wherein the adverse side effect is constipation.

Claim 115 (withdrawn). The method of claim 105, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 116 (withdrawn). The method of claim 105, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 117 (withdrawn). A method of controlling chronic pain without tolerance to a CNS-active agent comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing tolerance to the CNS-active agent, and wherein the drug transporter is an ABC drug transporter.

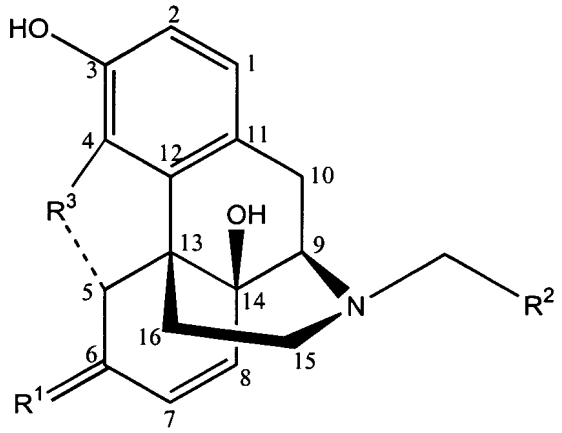
Claim 118 (withdrawn). The method of claim 117, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 119 (withdrawn). The method of claim 118, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 120 (withdrawn). The method of claim 117, further comprising administering to the patient an opioid receptor agonist.

Claim 121 (withdrawn). The method of claim 117, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop tolerance to the non-opioid CNS-active agent.

Claim 122 (withdrawn). The method of claim 117, wherein the inhibitor of the drug transporter is is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 123 (withdrawn). The method of claim 117, wherein the drug transporter is a P-glycoprotein.

Claim 124 (withdrawn). The method of claim 123, wherein the P-glycoprotein is PGP1a.

Claim 125 (withdrawn). The method of claim 120, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 126 (withdrawn). The method of claim 125, wherein the adverse side effect is constipation.

Claim 127 (withdrawn). The method of claim 117, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 128 (withdrawn). The method of claim 117, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 129 (withdrawn). A method of controlling chronic pain without tolerance to a CNS-active agent comprising co-administering to a patient :

(a) a sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing tolerance to the CNS-active agent, and wherein the drug transporter is an ABC drug transporter.

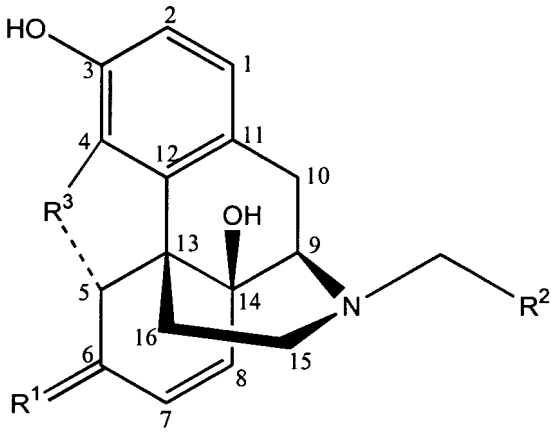
Claim 130 (withdrawn). The method of claim 129, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 131 (withdrawn). The method of claim 130, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 132 (withdrawn). The method of claim 129, further comprising administering to the patient an opioid receptor agonist.

Claim 133 (withdrawn). The method of claim 129, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop tolerance to the non-opioid CNS-active agent.

Claim 134 (withdrawn). The method of claim 129, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 135 (withdrawn). The method of claim 129, wherein the drug transporter is a P-glycoprotein.

Claim 136 (withdrawn). The method of claim 135, wherein the P-glycoprotein is PGP1a.

Claim 137 (withdrawn). The method of claim 132, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 138 (withdrawn). The method of claim 137, wherein the adverse side effect is constipation.

Claim 139 (withdrawn). The method of claim 129, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 140 (withdrawn). The method of claim 129, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 141 (withdrawn). A method of controlling chronic pain with a CNS-active agent without developing withdrawal comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing withdrawal, and wherein the drug transporter is an ABC drug transporter.

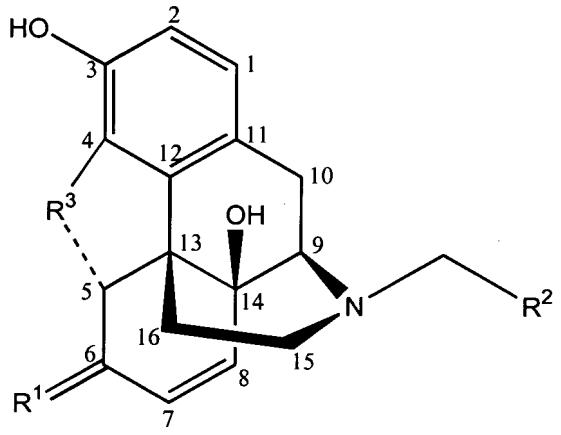
Claim 142 (withdrawn). The method of claim 141, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 143 (withdrawn). The method of claim 142, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 144 (withdrawn). The method of claim 141, further comprising administering to the patient an opioid receptor agonist.

Claim 145 (withdrawn). The method of claim 141, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop withdrawal to the non-opioid CNS-active agent.

Claim 146 (withdrawn). The method of claim 141, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 147 (withdrawn). The method of claim 141, wherein the drug transporter is a P-glycoprotein.

Claim 148 (withdrawn). The method of claim 147, wherein the P-glycoprotein is PGP1a.

Claim 149 (withdrawn). The method of claim 144, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 150 (withdrawn). The method of claim 149, wherein the adverse side effect is constipation.

Claim 151 (withdrawn). The method of claim 141, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 152 (withdrawn). The method of claim 141, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 153 (withdrawn). A method of controlling chronic pain with a CNS-active agent without developing withdrawal comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of a non-opioid CNS-active agent; and

(b) an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain,

wherein the co-administration of the inhibitor of the drug transporter with the non-opioid CNS-active agent prevents the patient from developing withdrawal, and wherein the drug transporter is an ABC drug transporter.

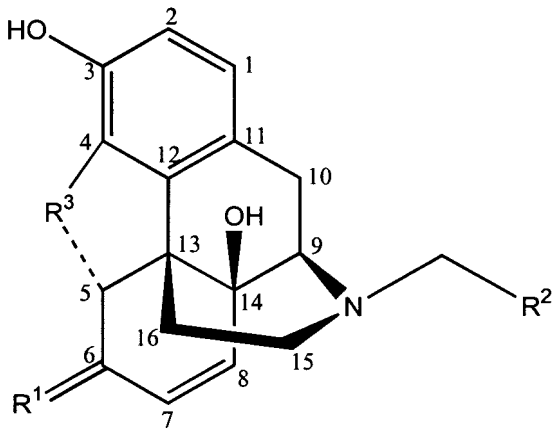
Claim 154 (withdrawn). The method of claim 153, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 155 (withdrawn). The method of claim 154, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 156 (withdrawn). The method of claim 153, further comprising administering to the patient an opioid receptor agonist.

Claim 157 (withdrawn). The method of claim 153, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop withdrawal to the non-opioid CNS-active agent.

Claim 158 (withdrawn). The method of claim 153, wherein the inhibitor of the drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 159 (withdrawn). The method of claim 153, wherein the drug transporter is a P-glycoprotein.

Claim 160 (withdrawn). The method of claim 159, wherein the P-glycoprotein is PGP1a.

Claim 161 (withdrawn). The method of claim 156, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 162 (withdrawn). The method of claim 161, wherein the adverse side effect is constipation.

Claim 163 (withdrawn). The method of claim 153, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 164 (withdrawn). The method of claim 153, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 165 (withdrawn). A method of preventing a patient from becoming tolerant to or dependent upon a non-opioid CNS-active agent comprising co-administering to the patient:

(a) an amount of an inhibitor of a drug transporter effective to reduce efflux of the non-opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter; and

(b) a therapeutic or sub-therapeutic dose of non-opioid CNS-active agent, thereby preventing the patient from becoming tolerant to or dependent upon the non-opioid CNS-active agent.

Claim 166 (withdrawn). The method of claim 165, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 167 (withdrawn). The method of claim 166, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 168 (withdrawn). The method of claim 165, further comprising administering to the patient an opioid receptor agonist.

Claim 169 (withdrawn). The method of claim 165, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop tolerance or dependence.

Claim 170 (withdrawn). The method of claim 165, wherein the drug transporter is a P-glycoprotein.

Claim 171 (withdrawn). The method of claim 170, wherein the P-glycoprotein is PGP1a.

Claim 172 (withdrawn). The method of claim 168, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 173 (withdrawn). The method of claim 172, wherein the adverse side effect is constipation.

Claim 174 (withdrawn). The method of claim 165, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 175 (withdrawn). The method of claim 165, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 176 (withdrawn). A method of preventing a patient from becoming tolerant to or dependent upon a non-opioid CNS-active agent comprising co-administering to the patient:

(a) an amount of an inhibitor of a drug transporter effective to increase the concentration of the non-opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter; and

(b) a therapeutic or sub-therapeutic dose of the non-opioid CNS-active agent, thereby preventing the patient from becoming tolerant to or dependent upon the non-opioid CNS-active agent.

Claim 177 (withdrawn). The method of claim 176, wherein the inhibitor of the drug transporter is an opioid receptor antagonist.

Claim 178 (withdrawn). The method of claim 172, wherein the opioid receptor antagonist is a compound selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 179 (withdrawn). The method of claim 176, further comprising administering to the patient an opioid receptor agonist.

Claim 180 (withdrawn). The method of claim 176, wherein the sub-therapeutic dose of the non-opioid CNS-active agent is less than the dose required to develop a drug dependence.

Claim 181 (withdrawn). The method of claim 176, wherein the drug transporter is a P-glycoprotein.

Claim 182 (withdrawn). The method of claim 181, wherein the P-glycoprotein is PGP1a.

Claim 183 (withdrawn). The method of claim 179, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 184 (withdrawn). The method of claim 183, wherein the adverse side effect is constipation.

Claim 185 (withdrawn). The method of claim 176, wherein the inhibitor of the drug transporter is a compound listed in Table 11.

Claim 186 (withdrawn). The method of claim 176, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

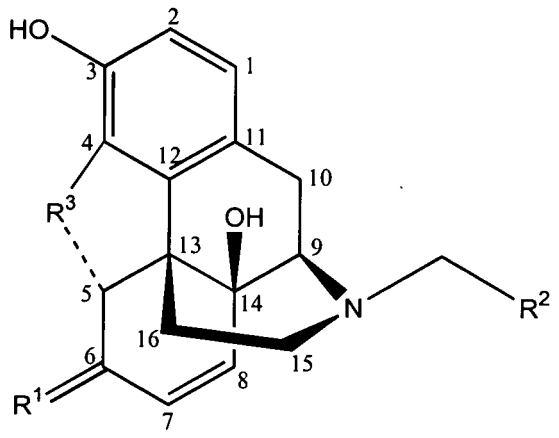
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 187 (withdrawn). A method of inhibiting a P-glycoprotein in a patient suffering from pain comprising administering to the patient a P-glycoprotein inhibiting amount of an inhibitor of an ABC drug transporter, wherein the inhibitor is selected from the group consisting of naltrexone, naloxone and nalmefene, wherein the inhibitor is administered before, with, or after the administration to the patient of a therapeutically effective amount of a non-opioid CNS-active agent.

Claim 188 (withdrawn). The method of claim 187, wherein the inhibitor is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 189 (withdrawn). A method of enhancing efficacy of an opioid CNS-active agent comprising:

co-administering to a patient a therapeutic dose of the opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter.

Claim 190 (withdrawn). The method of claim 189, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 191 (withdrawn). The method of claim 190, wherein the opioid receptor is selected from the group consisting of morphine and oxycodone.

Claim 192 (withdrawn). The method of claim 189, wherein the drug transporter is a P-glycoprotein.

Claim 193 (withdrawn). The method of claim 192, wherein the P-glycoprotein is PGP1a.

Claim 194 (withdrawn). The method of claim 189, further comprising administering to the patient an opioid receptor agonist.

Claim 195 (withdrawn). The method of claim 190, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 196 (withdrawn). The method of claim 195, wherein the adverse side effect is constipation.

Claim 197 (withdrawn). The method of claim 189, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 198 (withdrawn). The method of claim 189, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 199 (withdrawn). A method of enhancing efficacy of an opioid CNS-active agent comprising:

co-administering to a patient a sub-therapeutic dose of the opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to reduce

efflux of the non-opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter.

Claim 200 (withdrawn). The method of claim 199, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 201 (withdrawn). The method of claim 200, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 202 (withdrawn). The method of claim 199, wherein the drug transporter is a P-glycoprotein.

Claim 203 (withdrawn). The method of claim 202, wherein the P-glycoprotein is PGP1a.

Claim 204 (withdrawn). The method of claim 199, further comprising administering to the patient an opioid receptor agonist.

Claim 205 (withdrawn). The method of claim 200, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 206 (withdrawn). The method of claim 205, wherein the adverse side effect is constipation.

Claim 207 (withdrawn). The method of claim 199, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 208 (withdrawn). The method of claim 199, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 209 (withdrawn). A method of enhancing efficacy of an opioid CNS-active agent comprising:

co-administering to a patient a therapeutic dose of the opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to increase the concentration of the opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter.

Claim 210 (withdrawn). The method of claim 209, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 211 (withdrawn). The method of claim 210, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 212 (withdrawn). The method of claim 209, wherein the drug transporter is a P-glycoprotein.

Claim 213 (withdrawn). The method of claim 212, wherein the P-glycoprotein is PGP1a.

Claim 214 (withdrawn). The method of claim 209, further comprising administering to the patient an opioid receptor agonist.

Claim 215 (withdrawn). The method of claim 210, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 216 (withdrawn). The method of claim 215, wherein the adverse side effect is constipation.

Claim 217 (withdrawn). The method of claim 209, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 218 (withdrawn). The method of claim 209, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 219 (withdrawn). A method of enhancing efficacy of an opioid CNS-active agent comprising:

co-administering to a patient a sub-therapeutic dose of the opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to increase the concentration of the opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter.

Claim 220 (withdrawn). The method of claim 219, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 221 (withdrawn). The method of claim 220, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 222 The method of claim 219, wherein the drug transporter is a P-glycoprotein.

Claim 223 (withdrawn). The method of claim 222, wherein the P-glycoprotein is PGP1a.

Claim 224 (withdrawn). The method of claim 219, further comprising administering to the patient an opioid receptor agonist.

Claim 225 (withdrawn). The method of claim 220, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 226 (withdrawn). The method of claim 225, wherein the adverse side effect is constipation.

Claim 227 (withdrawn). The method of claim 219, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 228 (withdrawn). The method of claim 219, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 229 (withdrawn). A method of reversing tolerance to an opioid CNS-active agent comprising co-administering to a patient who is tolerant to the opioid CNS-active agent:

(a) an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid receptor agonist from the brain, wherein the drug transporter is an ABC drug transporter, and

(b) the opioid CNS-active agent to which the patient developed tolerance.

Claim 230 (withdrawn). The method of claim 229, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 231 (withdrawn). The method of claim 230, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 232 (withdrawn). The method of claim 229, wherein the drug transporter is a P-glycoprotein.

Claim 233 (withdrawn). The method of claim 232, wherein the P-glycoprotein is PGP1a.

Claim 234 (withdrawn). The method of claim 229, further comprising administering to the patient an opioid receptor agonist.

Claim 235 (withdrawn). The method of claim 230, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 236 (withdrawn). The method of claim 235, wherein the adverse side effect is constipation.

Claim 237 (withdrawn). The method of claim 229, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 238 (withdrawn). The method of claim 229, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 239 (withdrawn). A method of reversing tolerance to an opioid CNS-active agent comprising co-administering to a patient who is tolerant to the opioid CNS-active agent:

(a) an amount of a non-opioid inhibitor of a drug transporter effective to increase the concentration of the opioid receptor agonist in the brain, wherein the drug transporter is an ABC drug transporter, and

(b) the opioid CNS-active agent to which the patient developed tolerance.

Claim 240 (withdrawn). The method of claim 239, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 241 (withdrawn). The method of claim 240, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 242 (withdrawn). The method of claim 239, wherein the drug transporter is a P-glycoprotein.

Claim 243 (withdrawn). The method of claim 242, wherein the P-glycoprotein is PGP1a.

Claim 244 (withdrawn). The method of claim 239, further comprising administering to the patient an opioid receptor agonist.

Claim 245 (withdrawn). The method of claim 240, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 246 (withdrawn). The method of claim 245, wherein the adverse side effect is constipation.

Claim 247 (withdrawn). The method of claim 239, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 248 (withdrawn). The method of claim 239, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 249 (withdrawn). A method of treating a patient with chronic pain comprising:

repeatedly over a period of time, co-administering to a patient a therapeutic or sub-therapeutic dose of an opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain;

wherein the period of time is greater than the period of time in which the patient would develop tolerance to or develop dependence upon the opioid CNS-active agent

administered in the absence of the non-opioid inhibitor of the drug transporter, and wherein the drug transporter is an ABC drug transporter.

Claim 250 (withdrawn). The method of claim 249, wherein the period of time is greater than the period of time in which the patient would develop tolerance to the opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 251 (withdrawn). The method of claim 249, wherein the period of time is greater than the period of time in which the patient would develop dependence upon the opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 252 (withdrawn). The method of claim 249, further comprising administering to the patient an opioid receptor agonist.

Claim 253 (withdrawn). The method of claim 249, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 254 (withdrawn). The method of claim 253, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 255 (withdrawn). The method of claim 249, wherein the drug transporter is a P-glycoprotein.

Claim 256 (withdrawn). The method of claim 255, wherein the P-glycoprotein is PGP1a.

Claim 257 (withdrawn). The method of claim 250, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 258 (withdrawn). The method of claim 257, wherein the adverse side effect is constipation.

Claim 259 (withdrawn). The method of claim 249, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 260 (withdrawn). The method of claim 249, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 261 (withdrawn). A method of treating a patient with chronic pain comprising:

repeatedly over a period of time, co-administering to a patient a sub-analgesic dose of an opioid CNS-active agent and an amount of a non-opioid inhibitor of a drug transporter effective to increase the concentration of the opioid receptor agonist in the brain;

wherein the period of time is greater than the period of time in which the patient would develop tolerance to or develop dependence upon the opioid CNS-active agent administered in the absence of the non-opioid inhibitor of the drug transporter, and wherein the drug transporter is an ABC drug transporter.

Claim 262 (withdrawn). The method of claim 261, wherein the period of time is greater than the period of time in which the patient would develop tolerance to the

opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 263 (withdrawn). The method of claim 261, wherein the period of time is greater than the period of time in which the patient would develop dependence upon the opioid CNS-active agent administered in the absence of the inhibitor of the drug transporter.

Claim 264 (withdrawn). The method of claim 261, further comprising administering to the patient an opioid receptor agonist.

Claim 265 (withdrawn). The method of claim 261, wherein the non-opioid CNS-active agent is an opioid receptor agonist.

Claim 266 (withdrawn). The method of claim 265, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 267 (withdrawn). The method of claim 261, wherein the drug transporter is a P-glycoprotein.

Claim 268 (withdrawn). The method of claim 267, wherein the P-glycoprotein is PGP1a.

Claim 269 (withdrawn). The method of claim 262, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 270 (withdrawn). The method of claim 267, wherein the adverse side effect is constipation.

Claim 271 (withdrawn). The method of claim 261, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 272 (withdrawn). The method of claim 261, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 273 (withdrawn). A method of controlling chronic pain without dependence comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain,

wherein the drug transporter is an ABC drug transporter , and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-active agent prevents the patient from developing dependence upon the opioid CNS-active agent.

Claim 274 (withdrawn). The method of claim 273, wherein the sub-therapeutic dose of opioid CNS-active agent is less than the dose required to develop dependence upon the opioid CNS-active agent.

Claim 275 (withdrawn). The method of claim 273, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 276 (withdrawn). The method of claim 275, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 277 (withdrawn). The method of claim 273, wherein the drug transporter is a P-glycoprotein.

Claim 278 (withdrawn). The method of claim 277, wherein the P-glycoprotein is PGP1a.

Claim 279 (withdrawn). The method of claim 273, further comprising administering to the patient an opioid receptor agonist.

Claim 280 (withdrawn). The method of claim 274, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 281 (withdrawn). The method of claim 280, wherein the adverse side effect is constipation.

Claim 282 (withdrawn). The method of claim 273, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 283 (withdrawn). The method of claim 273, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 284 (withdrawn). A method of controlling chronic pain without dependence comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to increase concentration of the opioid CNS-active agent in the brain,

wherein the drug transporter is an ABC drug transporter, and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-active agent prevents the patient from developing dependence upon the opioid CNS-active agent.

Claim 285 (withdrawn). The method of claim 284, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop dependence upon the opioid CNS-active agent.

Claim 286 (withdrawn). The method of claim 284, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 287 (withdrawn). The method of claim 286, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 288 (withdrawn). The method of claim 284, wherein the drug transporter is a P-glycoprotein.

Claim 289 (withdrawn). The method of claim 288, wherein the P-glycoprotein is PGP1a.

Claim 290 (withdrawn). The method of claim 284, further comprising administering to the patient an opioid receptor agonist.

Claim 291 (withdrawn). The method of claim 285, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 292 (withdrawn). The method of claim 291, wherein the adverse side effect is constipation.

Claim 293 (withdrawn). The method of claim 284, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 294 (withdrawn). The method of claim 284, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 295 (withdrawn). A method of controlling chronic pain without tolerance comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain,

wherein the drug transporter is an ABC drug transporter, and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-

active agent prevents the patient from developing tolerance to the opioid CNS-active agent.

Claim 296 (withdrawn). The method of claim 295, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop tolerance to the opioid CNS-active agent.

Claim 297 (withdrawn). The method of claim 295, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 298 (withdrawn). The method of claim 297, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 299 (withdrawn). The method of claim 295, wherein the drug transporter is a P-glycoprotein.

Claim 300 (withdrawn). The method of claim 299, wherein the P-glycoprotein is PGP1a.

Claim 301 (withdrawn). The method of claim 295, further comprising administering to the patient an opioid receptor agonist.

Claim 302 (withdrawn). The method of claim 296, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 303 (withdrawn). The method of claim 302, wherein the adverse side effect is constipation.

Claim 304 (withdrawn). The method of claim 295, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 305 (withdrawn). The method of claim 295, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 306 (withdrawn). A method of controlling chronic pain without tolerance comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to increase concentration of the opioid CNS-active agent in the brain,

wherein the drug transporter is an ABC drug transporter, and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-active agent prevents the patient from developing tolerance to the opioid CNS-active agent.

Claim 307 (withdrawn). The method of claim 306, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop tolerance to the opioid CNS-active agent.

Claim 308 (withdrawn). The method of claim 306, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 309 (withdrawn). The method of claim 308, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 310 (withdrawn). The method of claim 306, wherein the drug transporter is a P-glycoprotein.

Claim 311 (withdrawn). The method of claim 310, wherein the P-glycoprotein is PGP1a.

Claim 312 (withdrawn). The method of claim 306, further comprising administering to the patient an opioid receptor agonist.

Claim 313 (withdrawn). The method of claim 307, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 314 (withdrawn). The method of claim 313, wherein the adverse side effect is constipation.

Claim 315 (withdrawn). The method of claim 306, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 316 (withdrawn). The method of claim 306, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 317 (withdrawn). A method of controlling chronic pain without withdrawal comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain,

wherein the drug transporter is an ABC drug transporter, and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-active agent prevents the patient from developing withdrawal.

Claim 318 (withdrawn). The method of claim 317, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop withdrawal.

Claim 319 (withdrawn). The method of claim 317, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 320 (withdrawn). The method of claim 319, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 321 (withdrawn). The method of claim 317, wherein the drug transporter is a P-glycoprotein.

Claim 322 (withdrawn). The method of claim 321, wherein the P-glycoprotein is PGP1a.

Claim 323 (withdrawn). The method of claim 317, further comprising administering to the patient an opioid receptor agonist.

Claim 324 (withdrawn). The method of claim 318, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 325 (withdrawn). The method of claim 324, wherein the adverse side effect is constipation.

Claim 326 (withdrawn). The method of claim 317, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 327 (withdrawn). The method of claim 317, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 328 (withdrawn). A method of controlling chronic pain without withdrawal comprising co-administering to a patient:

(a) a therapeutic or sub-therapeutic dose of an opioid CNS-active agent; and

(b) an amount of a non-opioid inhibitor of a drug transporter effective to increase concentration of the opioid CNS-active agent in the brain,

wherein the drug transporter is an ABC drug transporter, and wherein the co-administration of the non-opioid inhibitor of the drug transporter with the opioid CNS-active agent prevents the patient from developing withdrawal.

Claim 329 (withdrawn). The method of claim 328, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop withdrawal.

Claim 330 (withdrawn). The method of claim 328, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 331 (withdrawn). The method of claim 330, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 332 (withdrawn). The method of claim 328, wherein the drug transporter is a P-glycoprotein.

Claim 333 (withdrawn). The method of claim 332, wherein the P-glycoprotein is PGP1a.

Claim 334 (withdrawn). The method of claim 328, further comprising administering to the patient an opioid receptor agonist.

Claim 335 (withdrawn). The method of claim 329, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 336 (withdrawn). The method of claim 335, wherein the adverse side effect is constipation.

Claim 337 (withdrawn). The method of claim 328, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 338 (withdrawn). The method of claim 328, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 339 (withdrawn). A method of preventing a patient from becoming tolerant to or dependent upon an opioid CNS-active agent comprising co-administering to the patient:

(a) an amount of a non-opioid inhibitor of a drug transporter effective to reduce efflux of the opioid CNS-active agent from the brain, wherein the drug transporter is an ABC drug transporter; and

(b) a therapeutic or sub-therapeutic dose of the opioid CNS-active agent, thereby preventing the patient from becoming tolerant to or dependent upon the opioid CNS-active agent.

Claim 340 (withdrawn). The method of 339, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop tolerance to or dependence upon the opioid CNS-active agent.

Claim 341 (withdrawn). The method of claim 339, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 342 (withdrawn). The method of claim 341, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 343 (withdrawn). The method of claim 339, wherein the drug transporter is a P-glycoprotein.

Claim 344 (withdrawn). The method of claim 343, wherein the P-glycoprotein is PGP1a.

Claim 345 (withdrawn). The method of claim 339, further comprising administering to the patient an opioid receptor agonist.

Claim 346 (withdrawn). The method of claim 340, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 347 (withdrawn). The method of claim 346, wherein the adverse side effect is constipation.

Claim 348 (withdrawn). The method of claim 339, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 349 (withdrawn). The method of claim 339, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 350 (withdrawn). A method of preventing a patient from becoming tolerant to or dependent upon an opioid CNS-active agent comprising co-administering to the patient:

(a) an amount of a non-opioid inhibitor of a drug transporter effective to increase the concentration of the opioid CNS-active agent in the brain, wherein the drug transporter is an ABC drug transporter; and

(b) administering to the patient a therapeutic or sub-therapeutic dose of the opioid CNS-active agent, thereby preventing the patient from becoming tolerant to or dependent upon the opioid CNS-active agent.

Claim 351 (withdrawn). The method of claim 350, wherein the sub-therapeutic dose of the opioid CNS-active agent is less than the dose required to develop tolerance to or dependence upon the CNS-active agent.

Claim 352 (withdrawn). The method of claim 350, wherein the opioid CNS-active agent is an opioid receptor agonist.

Claim 353 (withdrawn). The method of claim 352, wherein the opioid receptor agonist is selected from the group consisting of morphine and oxycodone.

Claim 354 (withdrawn). The method of claim 350, wherein the drug transporter is a P-glycoprotein.

Claim 355 (withdrawn). The method of claim 354, wherein the P-glycoprotein is PGP1a.

Claim 356 The method of claim 350, further comprising administering to the patient an opioid receptor agonist.

Claim 357 (withdrawn). The method of claim 351, wherein an adverse side effect associated with the administration of the opioid receptor agonist is attenuated by the non-opioid inhibitor of the drug transporter.

Claim 358 (withdrawn). The method of claim 357, wherein the adverse side effect is constipation.

Claim 359 (withdrawn). The method of claim 350, wherein the non-opioid inhibitor of the drug transporter is a compound listed in Table 11.

Claim 360 (withdrawn). The method of claim 350, wherein the inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 361 (withdrawn). A composition comprising:

(a) an opioid receptor agonist; and

(b) a non-opioid compound

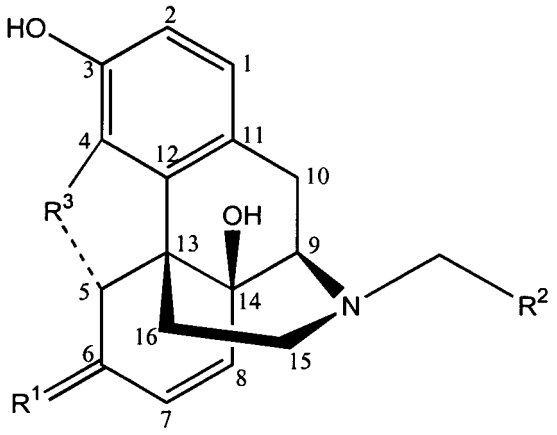
wherein the non-opioid compound is capable of inhibiting a drug transporter, wherein the drug transporter is an ABC drug transporter.

Claim 362 (currently amended). A composition comprising

(a) a non-opioid CNS-active agent; and

(b) an opioid receptor antagonist in an amount in the range of from **3 ng/kg to 3000 ng/kg** ~~**0.0001 μM to 100 μM**~~.

Claim 363 (original). The composition of claim 362, wherein the opioid receptor antagonist is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

Claim 364 (currently amended). A composition comprising

(a) a non-opioid CNS-active agent; and

(b) an ABC drug transporter protein-inhibiting amount of an opioid inhibitor of an ABC drug transporter in an amount in the range of from **3 ng/kg to 3000 ng/kg** ~~**0.0001 μM to 100 μM**~~.

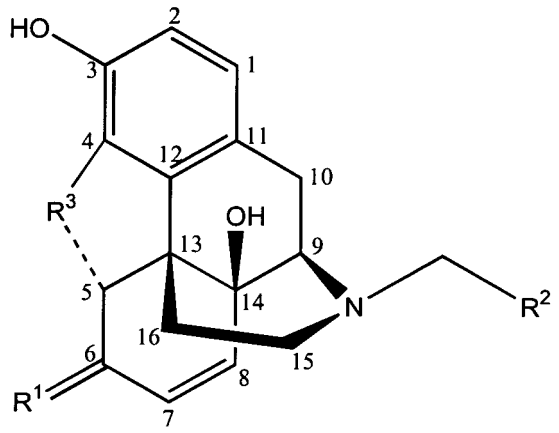
Claim 365 (original). The composition of claim 364, wherein the ABC drug transporter is a PGP drug transporter.

Claim 366 (original). The composition of claim 365, wherein the PGP drug transporter is a PGP1a drug transporter.

Claim 367 (original). The composition of claim 364, wherein the opioid inhibitor is an opioid receptor antagonist.

Claim 368 (original). The composition of claim 367, wherein the opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, and nalmefene.

Claim 369 (original). The composition of claim 364, wherein the inhibitor is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 370 (withdrawn). A composition comprising

(a) an opioid CNS-active agent; and

(b) a non-opioid inhibitor of an ABC drug transporter.

Claim 371 (withdrawn). The composition of claim 370, wherein the ABC drug transporter is a PGP drug transporter.

Claim 372 (withdrawn). The composition of claim 371, wherein the PGP drug transporter is a PGP1a drug transporter.

Claim 373 (currently amended). A composition comprising:

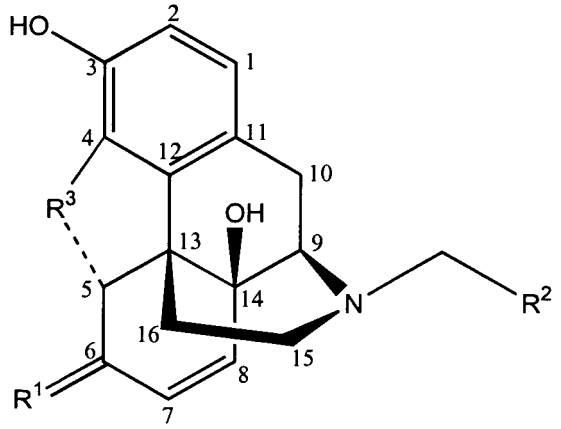
(a) a non-opioid CNS-active agent, and

(b) an ABC drug transporter protein-inhibiting amount of an opioid receptor antagonist that is an inhibitor of an ABC drug transporter, wherein the amount is in the range of from **3 ng/kg to 3000 ng/kg** ~~**0.0001 μM to 100 μM**~~;
wherein the composition is for the treatment of chronic pain, for controlling pain without dependence, tolerance, or withdrawal.

Claim 374 (original). The composition of claim 373, wherein the opioid receptor antagonist is selected from the group consisting of naltrexone, naloxone, and nalmefene.

Claim 375 (previously presented). The composition of claim 373, wherein the non-opioid CNS-active agent is selected from the group consisting of diazepam, lithium, triazolam, and zolpidem.

Claim 376 (original). The composition of claim 373, wherein the opioid receptor antagonist is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH.

Claim 377 (withdrawn). A method of identifying a compound suitable for co-administration with a CNS-active agent for enhanced efficacy of the CNS-active agent, the method comprising:

(a) assaying a test compound for inhibition of an ABC drug transporter by

(i) applying a known inhibitor of the ABC drug transporter to an ABC drug transporter barrier in the in the presence and absence of the test compound, and

(ii) comparing the concentration of the known inhibitor that has been transported across the ABC drug transporter in the presence of the test compound with the concentration of the known inhibitor that has been transported across the ABC drug transporter barrier in the absence of the test compound, and

(b) selecting the test compound if the concentration of the known inhibitor that has been transported across the ABC drug transporter in the presence of the test compound is decreased relative to the concentration of the known inhibitor that has been transported across the ABC drug transporter barrier in the absence of the test compound,

wherein the known inhibitor is selected from the group consisting of naltrexone, nalmefene and naloxone.

Claim 378 (withdrawn). The method of claim 377, wherein the step of assaying a test compound comprises screening a library of test compounds.

Claim 379 (withdrawn). The method of claim 377, wherein the ABC drug transporter is a P-glycoprotein.

Claim 380 (withdrawn). The method of claim 379, wherein the P-glycoprotein is PGP1a.

Claim 381 (withdrawn). The method of claim 377, wherein the CNS-active agent is a non-opioid.

Claim 382 (withdrawn). The method of claim 381, wherein the selected test compound is opioid.

Claim 383 (withdrawn). The method of claim 377, wherein the CNS-active agent is an opioid and the selected test compound is a non-opioid.

Claim 384 (withdrawn). A method of identifying a compound suitable for co-administration with a CNS-active agent for enhanced efficacy of the CNS-active agent, the method comprising:

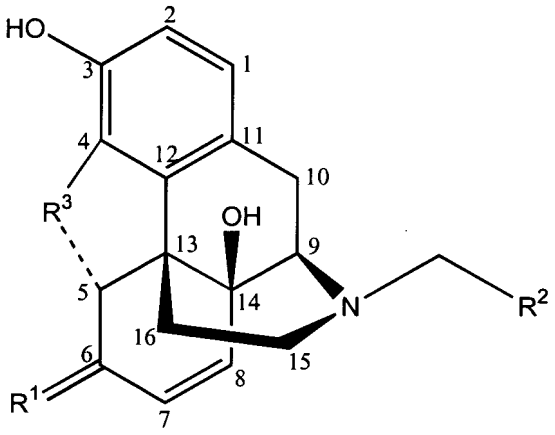
(a) assaying a test compound for inhibition of an ABC drug transporter by

(i) applying a known inhibitor of the ABC drug transporter to an ABC drug transporter barrier in the in the presence and absence of the test compound, and

(ii) comparing the concentration of the known inhibitor that has been transported across the ABC drug transporter in the presence of the test compound with the concentration of the known inhibitor that has been transported across the ABC drug transporter barrier in the absence of the test compound, and

(b) selecting the test compound if the concentration of the known inhibitor that has been transported across the ABC drug transporter in the presence of the test compound is decreased relative to the concentration of the known inhibitor that has been transported across the ABC drug transporter barrier in the absence of the test compound,

wherein the known inhibitor is a compound of the formula:



wherein R^1 is CH_2 or O;
wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and
wherein R^3 is O, CH_2 or NH.

Claim 385 (withdrawn). The method of claim 384, wherein the step of assaying a test compound comprises screening a library of test compounds.

Claim 386 (withdrawn). The method of claim 384, wherein the ABC drug transporter is a P-glycoprotein.

Claim 387 (withdrawn). The method of claim 386, wherein the P-glycoprotein is PGP1a.

Claim 388 (withdrawn). The method of claim 384, wherein the CNS-active agent is a non-opioid.

Claim 389 (withdrawn). The method of claim 388, wherein the selected test compound is opioid.

Claim 390 (withdrawn). The method of claim 384, wherein the CNS-active agent is an opioid and the selected test compound is a non-opioid.

Claim 391 (withdrawn). A method of identifying a compound as a therapeutic agent for transport across the blood brain barrier comprising:

(a) identifying a therapeutic agent which is active in the brain;

(b) assaying the ability of the therapeutic agent to be transported across a membrane by an ABC drug transporter; and

(c) repeating the transport assay to determine whether addition of an opioid receptor antagonist inhibits transport of the therapeutic agent across the membrane, whereby the compound which is active in the brain, is transported by an ABC protein and whose ABC protein-mediated transport is inhibited by the opioid receptor antagonist is identified as a compound for transport across the blood brain barrier.

Claim 392 (withdrawn). The method of claim 391, wherein the opioid receptor antagonist is nalmefene, naloxone, or naltrexone.

Claim 393 (withdrawn). A method of enhancing the potency of a compound identified by the method of claim 391 comprising:

co-administering a therapeutic amount of the compound and an amount of an opioid receptor antagonist capable of inhibiting a drug transporter, wherein the amount of the opioid receptor antagonist is sufficient to reduce transport of the compound across a biological membrane.